



Science Ambassador 2016 Lesson Plan

What's in the Syringe? A Fungal Meningitis Outbreak Investigation

Overview

Students will investigate a multistate fungal meningitis outbreak and explore some of the roles of a public health outbreak response team. A jigsaw activity is used to help students organize findings of the investigation, according to essential elements of information (EEI). The jigsaw technique is a teaching method in which groups work on small problems that the class collates into a final outcome. EEI is situational information about people, systems, and services that is critical for an effective outbreak response. Students use findings to create a case definition. Then, students develop a communication tool to alert and inform the public about the outbreak. This lesson is intended for high school students in grades 9–12.

Learning Objectives

After completing this lesson, students should be able to

- Describe how EEI is used during a public health outbreak response,
- Characterize an outbreak,
- Create a case definition, and
- Develop a communication tool (containing clinical information, risk factors about the fungal meningitis outbreak, and suggested actions for those who might have been exposed) for a variety of audiences.

Duration

This lesson plan can be taught as one 90-minute session or two 45-minute sessions.



Authors

This lesson plan was developed by teachers in the Science Ambassador Workshop, an annual career workforce training for science, math, and health science teachers. For more information, visit <http://www.cdc.gov/careerpaths/scienceambassador>.

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What's in the Syringe? A Fungal Meningitis Outbreak Investigation

Background

In September 2012, the Centers for Disease Control and Prevention (CDC), in collaboration with state and local health departments and the Food and Drug Administration (FDA), began investigating a multistate outbreak of fungal meningitis and other infections among patients who received contaminated, preservative-free, methylprednisolone acetate (MPA) steroid injections from the New England Compounding Center in Framingham, Massachusetts. Active case-finding efforts and extensive investigation into medications and medication lot numbers received by patients were used to evaluate the source of infection.

Fungal meningitis is not spread from person to person.

Fungal meningitis can develop after a fungus spreads through the bloodstream from somewhere else in the body to the brain or spinal cord or from an infection next to the brain or spinal cord.

Signs and symptoms of fungal meningitis include fever, headache, stiff neck, nausea and vomiting, photophobia, and altered mental status.

If meningitis is suspected, samples of blood or cerebrospinal fluid (fluid surrounding the spinal cord) are collected and sent to a laboratory for testing. Knowing the specific cause of meningitis is important because the severity of illness and the treatment depend on the cause. To confirm fungal meningitis, specific laboratory tests can be performed, depending on the type of fungus suspected.¹ The predominant fungus identified in patients was *Exserohilum rostratum*.²

Summary

In this lesson, students role play as epidemiologists to investigate the multistate fungal meningococcal outbreak and explore some of the roles of the public health outbreak response team. A jigsaw activity is used to help students organize the findings of the investigation according to essential elements of information (EEI). The jigsaw technique is a teaching method in which groups work on small problems that the class collates into a final outcome. EEI is situational information about people, systems, and services that is critical for an effective outbreak response. Students use their EEI findings to create a case definition. Then, students role play as risk communication specialists to develop a communication tool to alert and inform the public about the outbreak.

This lesson is intended for biology-related courses with students in grades 9–12. It can also be used in lessons concerning epidemiology and public health emergency response. Students should already have a basic knowledge of types of pathogens.



Figure 1: This photomicrograph reveals some of the morphology of the fungal organism, *Exserohilum rostratum*. CDC PHIL ID#15143

¹ More information on fungal meningitis can be found at <http://www.cdc.gov/meningitis/fungal.html>.

² More information on this outbreak can be found at <http://www.cdc.gov/hai/outbreaks/meningitis.html>.

Part 1: Identifying the Essential Elements of Information in a Fungal Meningitis Outbreak (45 minutes)

Preparation

Before Part 1,

- Assign Worksheet 1A, Part A for homework. Students read the scenario and research definitions for key terms. See materials.
- Review online resources as needed. See online resources.

Materials

- Worksheet 1A: What's in the Syringe?
Description: This worksheet provides students with information on a multistate fungal meningitis outbreak that occurred in 2012. Students will use this information to complete EEI flowcharts. Then, students will combine the information into one larger flowchart and create a case definition. At the end of the activity, students will use this information to create a communication tool.
- Worksheet 1B: What's in the Syringe?, Guide
Description: The guide provides sample answers for the student worksheet.
- Sticky notes and large paper.

Online Resources

- Multistate Outbreak of Fungal Meningitis and Other Infections – Case Count
http://www.cdc.gov/hai/outbreaks/meningitis-map-large.html#casecount_table
Description: This resource was used to develop the fungal meningitis outbreak data tables.
- Update: Multistate Infections of Fungal Meningitis and Joint Infections Associated with Contaminated Steroid Medications
<http://emergency.cdc.gov/HAN/han00329.asp>
Description: This resource provides details of the fungal meningitis outbreak of 2012 that this lesson was based on.
- Multistate Outbreak of Fungal Infection Associated with Injection of Methylprednisolone Acetate Solution from a Single Compounding Pharmacy – United States, 2012.
<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6141a4.htm>
Description: This resource was used to develop the fungal Meningitis outbreak data tables.
- Fungal Meningitis
<http://www.cdc.gov/meningitis/fungal.html>
Description: This resource provides general information about fungal meningitis, including its cause, transmission, symptoms, and preventative measures.

Activity

1. Review the key terms completed for homework on Worksheet 1A, Part A.
2. Introduce EEI as a method to organize findings of an investigation. Explain that EEI is situational information about people, systems, and services that is critical for an effective outbreak response.
3. Assign Worksheet 1A, Part B: Outbreak information
 - a. Read through the scenario as a class.
4. Assign Worksheet 1A, Part C: Essential Elements of Investigation flowcharts
 - a. Divide students into groups of five. Then, assign each group member a team number 1-5.
 - b. Explain that each group will investigate the outbreak using the information provided, as if it were happening in real time. Explain that each group member will be assigned to investigate certain aspects of the outbreak with their team. Then, after all teams have completed their investigation, the group will collate their findings.
 - c. Explain the role of each of the five teams and how they will contribute to an epidemiologic response. Teams will investigate various components of the outbreak on the basis of the EEI: who is affected by the disease (Team 1: Who Is Affected?), geography of the disease (Team 2: Where Are the Cases?), clinical presentation of the disease (Team 3: What Is the Problem?), possible impact of the outbreak (Team 4: What Is the Risk?), and cause of the outbreak (Team 5: When and Why Is This Happening?).
 - d. Assign teams to complete the information on their team's section of the flowchart.
5. Assign Worksheet 1A, Part D: Putting it all together,
 - a. Instruct students to return to their original group.
 - b. Have each group collate their EEI flowchart together by taping the sections together.
 - c. Instruct students to create a case definition for the outbreak by using the information collected. Remind students that a case definition should include clinical symptoms, time of exposure, place of exposure, and persons to be investigated.
 - d. Ask for a student volunteer from each group to write their case definition on the board or a large sheet of paper in front of the class.
 - e. Provide students with sticky notes. Ask students to provide constructive criticism for two case definitions not including their own.
 - f. Lead a discussion about the characteristics of a case study definition and how it might change over time. The class should then come to a consensus on a case study definition.
 - g. Assign students to complete the critical thinking section and methods assessment with their group.
8. Divide students into two new groups: investigation justified and investigation not justified.
 - a. Have each group write at least three statements that would justify their position.
 - b. Have a student volunteer from each group present the statements for each position.
 - c. Provide each group five minutes to refute the other group's statements. Explain that justification for responding to an outbreak can be complicated and there are many factors involved. Note that for CDC to respond, the state public health department is required to request CDC support.
9. Bring students back to the initial scenario about Tom, the injured basketball player. Ask students if presenting Tom with the EEI flowchart would be effective in helping him understand his parents' concerns about receiving a steroid shot.

Part 2: Using Communication Techniques to Inform the Public (45 minutes)

Preparation

Before Part 2,

- Review the online resources for additional information on the outbreak investigation, if desired.

Materials

- **Worksheet 1A: What's in the Syringe?**
Description: This worksheet provides students with information on a multistate fungal meningitis outbreak that occurred in 2012. Students will use this information to complete EEI flowcharts. Then, students will combine the information into one larger flowchart and create a case definition. At the end of the activity, students will use this information to create a communication tool.
- **Worksheet 1B: What's in the Syringe?, Guide**
Description: The guide provides sample answers for the student worksheet.
- Artistic materials or technology that aids students in the creation of their communication tools.

Online Resources

- **Multistate Fungal Meningitis Outbreak Investigation**
<https://www.cdc.gov/hai/widgets/widgets.html>
Description: This web page gives an example of a communication tool released by CDC for the general public to promote action and awareness for a number of healthcare-associated infection topics and campaigns.

Activity

1. Recap the scenario, the completed EEI flowchart, and epidemiologic methods used. Explain to students that in Part E, they will use communication tools to present their findings to the public.
2. Introduce the idea that the CDC often uses a variety of communication formats to alert the public about risk factors or to make recommendations about how to prevent an outbreak from spreading. Communication tools can include infographics, video messages, social media, and podcasts.
3. Ask students to name some target audiences that might need information about the outbreak. Categorize their answers on the board. Sample categories include “directly affected” (e.g., patients or family members of patients who recently received steroid shots, doctors who recently provided steroid shots), “general public,” and “medical community”. Ask students which categories Tom, the high school senior who is considering receiving a steroid shot, and his doctor might fall into.
4. Assign students to groups. Assign target audiences to each group. Have students create a communication tool according to the rubric provided.
5. Have each group present their communication tool. Ask each group to explain their intended audience and who in the scenario the communication tool might be most suited for. (i.e., who was the tool most suited for: Tom, Tom's doctor, or Tom's parents?)

Educational Standards

The following CDC Epidemiology and Public Health Science (EPHS) Core Competencies for High School Students,¹ Next Generation Science Standards* (NGSS) Science & Engineering Practices,² and NGSS Cross-cutting Concepts³ are addressed:

HS-EPHS1-2. Discuss how epidemiologic thinking and a public health approach are used to transform a narrative into an evidence-based explanation.

NGSS Key Science & Engineering Practice²

Obtaining, Evaluating, and Communicating Information

Communicate scientific or technical information or ideas (e.g., phenomena or the process of development and the design and performance of a proposed process or system) in multiple formats (i.e., orally, graphically, textually, and mathematically).

NGSS Key Crosscutting Concept²

Cause and Effect

Empirical evidence is required to differentiate between cause and correlation and make claims about specific causes and effects.

HS-EPHS1-3 Apply epidemiologic thinking and a public health approach to a model (e.g., outbreak) to explain cause and effect associations that influence health and disease.

NGSS Key Science & Engineering Practice²

Developing and Using Models

Develop, revise, or use a model that is based on evidence to illustrate or predict relationships between systems or between components of a system.

NGSS Key Crosscutting Concept²

Cause and Effect

Cause and effect relationships can be suggested and predicted for complex natural and human designed systems by examining what is known about smaller scale mechanisms within the system.

HS-EPHS2-3 Use models (e.g., mathematical models, and figures) that are based on empirical evidence to identify patterns of health and disease to characterize a public health problem.

NGSS Key Science & Engineering Practice²

Analyze and Interpreting Data

Analyze data tools, technologies, or models (e.g., computational and mathematical) in order to make a valid and reliable scientific claim or determine an optimal design solution.

NGSS Key Crosscutting Concept²

Patterns

Mathematical representations are needed to identify some patterns. Empirical evidence is needed to identify patterns.

¹ Centers for Disease Control and Prevention (CDC). Science Ambassador Workshop—Epidemiology and Public Health Science: Core Competencies for high school students. Atlanta, GA: US Department of Health and Human Services, CDC; 2015.

² NGSS Lead States. Next Generation Science Standards: For States, By States (Appendix F—Science and Engineering Practices, Appendix G—Crosscutting Concepts). Achieve, Inc. on behalf of the twenty-six states and partners that collaborated on the NGSS. 2013. Available at: <http://www.nextgenscience.org/get-to-know>.

* Next Generation Science Standards is a registered trademark of Achieve. Neither Achieve nor the lead states and partners that developed the Next Generation Science Standards was involved in the production of, and does not endorse, this product.

Appendices

Worksheet 1A

What's in the Syringe?

Name: _____

Date: _____

Directions: Use this page to help you complete the activity and find definitions for key terms.

Scenario: Help! Is it Safe for Me to Have Steroid Injections?

Tom, a high school senior, is the star basketball player and has suffered a knee injury. The doctor has suggested a steroid injection to decrease swelling on his knee. Tom's parents recently heard about contaminated steroid injections on the news. CDC had just released its findings about a multistate outbreak of fungal meningitis among patients who received contaminated steroid injections from the New England Compounding Center. Tom's parents are concerned about him receiving a steroid injection. They prefer to find an alternative method for treatment. Tom is frustrated. He has not heard about the contaminated steroid injections and wants to get back to playing basketball. Tom decides to call his cousin who is a CDC epidemiologist to learn more about the outbreak.

You are Tom's cousin and decide to use the Essential Elements of Information (EEI) to organize the details of the fungal meningitis investigation for Tom. EEI is situational information about people, systems, and services that is critical for an effective outbreak response. EEI flowcharts are completed as epidemiologists answer who, what, when, where, and why questions of an outbreak, and ultimately help the response team design a case definition and control the outbreak.

Task

Your task is to help Tom show his parents that it will be safe to have a steroid injection.

Part A: Key Terms (Homework)

Directions: Use the CDC website to define each key term.

Case Definition

Epidemiologist

Meningitis

Fungal Meningitis

Outbreak

Risk Communication Specialist

Steroid Injection

Part B: Outbreak Information

Directions: Review the outbreak information provided. Use this information to complete Part C.

Fungal Meningitis Outbreak – Key Information

In September 2012, the Centers for Disease Control and Prevention (CDC), in collaboration with state and local health departments and the Food and Drug Administration (FDA), began investigating a multistate outbreak of fungal meningitis and other infections among patients who received contaminated preservative-free methylprednisolone acetate (MPA) steroid injections from the New England Compounding Center in Framingham, Massachusetts. Active case-finding efforts and extensive investigation into medications and medication lot numbers received by patients were used to evaluate the source of infection.

Fungal meningitis is not spread from person to person. Fungal meningitis can develop after a fungus spreads through the bloodstream from somewhere else in the body to the brain or spinal cord or from an infection next to the brain or spinal cord.

Signs and symptoms of fungal meningitis include fever, headache, stiff neck, nausea and vomiting, photophobia, and altered mental status.

If meningitis is suspected, samples of blood or cerebrospinal fluid (fluid surrounding the spinal cord) are collected and sent to a laboratory for testing. Knowing the specific cause of meningitis is important because the severity of illness and the treatment depend on the cause. To confirm fungal meningitis, specific lab tests can be performed, depending on the type of fungus suspected.³ The predominant fungus identified in patients is *Exserohilum rostratum*.⁴ See table 3.



Figure 2: This photomicrograph reveals some of the morphology of the fungal organism, *Exserohilum rostratum*. CDC PHIL ID#15143

³ More information on fungal meningitis can be found at: <http://www.cdc.gov/meningitis/fungal.html>.

⁴ More information on this outbreak can be found at: <http://www.cdc.gov/hai/outbreaks/meningitis.html>.

Table 1: Characteristics of patients (N = 70) with fungal infections following epidural steroid injection of methylprednisolone acetate from New England Compounding Center — United States, 2012.⁵

Characteristic	Number	(%)
Median age (yrs) (range)	68 (Range: 23-91)	
Sex		
Male	22	31
Female	48	69
Signs and Symptoms		
Headache	57	81
Fever	24	34
Nausea	21	30
Photophobia	7	10
Gait disturbance	3	4
Falls	8	11
Stroke	12	17
Fungus Identified		
Exserohilum species	13	9
Aspergillus species	1	1

Table 2: Cases and deaths with fungal infections linked to steroid injections – meningitis only cases.⁶

State		
TOTAL	234	64
Georgia (GA)	1	0
Illinois (IL)	2	0
Maryland (MD)	23	3
Minnesota (MN)	10	1
New Hampshire (NH)	9	0
New York (NY)	0	0
Pennsylvania (PA)	1	0
South Carolina (SC)	2	0
Texas (TX)	2	0
West Virginia (WV)	0	0

⁵This table was derived from: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6141a4.htm>.

⁶ The complete data table is available at: <http://www.cdc.gov/hai/outbreaks/meningitis-map-large.html>

Table 3: CDC laboratory-confirmed organisms from recalled New England Compounding Center lots of preservative-free methylprednisolone acetate (MPA) lots recalled on September 26, 2012.⁷

MPA Lot #	Beyond Use	Fungi Isolated	Description
06292012@26	12/26/2012	<i>Exserohilum rostratum</i>	Known to cause human disease
08102012@51	2/6/2013	<i>Exserohilum rostratum</i>	Known to cause human disease
08102012@51	2/6/2013	<i>Cladosporium cladosporioides</i>	Does not grow at human body temperature
06292012@26	12/26/2012	<i>Rhodotorula laryngis</i>	Does not grow at human body temperature Not known to cause human disease
08102012@51	2/6/2013	<i>Rhodotorula laryngis</i>	Does not grow at human body temperature Not known to cause human disease
08102012@51	2/6/2013	<i>Rhizopus stolonifer</i>	Does not grow at human body temperature. Not known to cause human disease

Fungal Meningitis Outbreak – FDA News Release

FDA reports conditions observed at New England Compounding Center facility – Oct. 26, 2012

Today, the U.S. Food and Drug Administration released a copy of the FDA Form 483 issued to the New England Compounding Center (NECC). The FDA observed and has since confirmed contaminated products and listed a number of observations regarding conditions in the clean room at NECC’s Framingham, Mass. facility.

The investigators also observed problems with NECC’s ability to maintain its clean room, which is the enclosed space that is designed and maintained to have a controlled environment with low levels of airborne particles and surface contamination. Production of sterile drug products in a properly functioning and maintained clean room reduces the risk of the introduction of microbial contamination into the drug during processing, including filling into its final container.

The FDA issues a 483 at the end of an inspection when the investigators believe that they observed conditions or practices that, in their judgment, may indicate violations of the Federal Food, Drug, and Cosmetic Act, or related regulations. The 483 does not constitute a final FDA determination that any observation listed on the 483 is a violation of the Federal Food, Drug, and Cosmetic Act or any related regulations.

The FDA considers the 483 along with an Establishment Inspection Report (EIR), prepared by FDA investigators, and any other relevant information, including any responses received by the company. The agency then considers whether further action, if any, is appropriate. The inspection report for NECC has not been completed and is not being shared at this time.

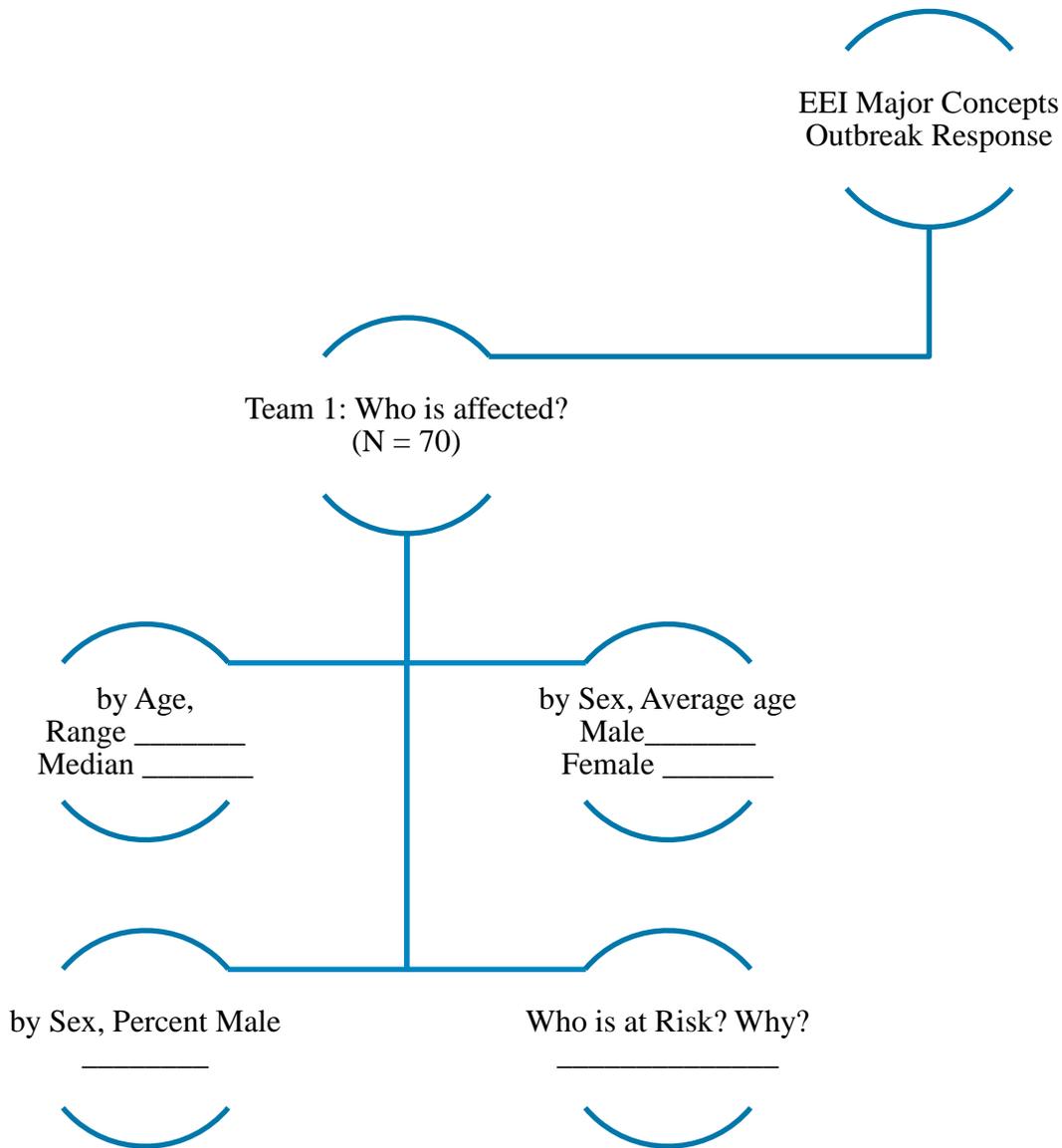
The FDA continues to work closely with the U.S. Centers for Disease Control and Prevention and state partners, including the Massachusetts Board of Registration in Pharmacy, to investigate the outbreak of fungal meningitis among patients who received NECC’s compounded preservative-free methylprednisolone acetate (80mg/ml), an injectable steroid.

⁷ This data is available at: <http://www.cdc.gov/hai/outbreaks/laboratory/index.html>.

Part C: Essential Elements of Information flowcharts

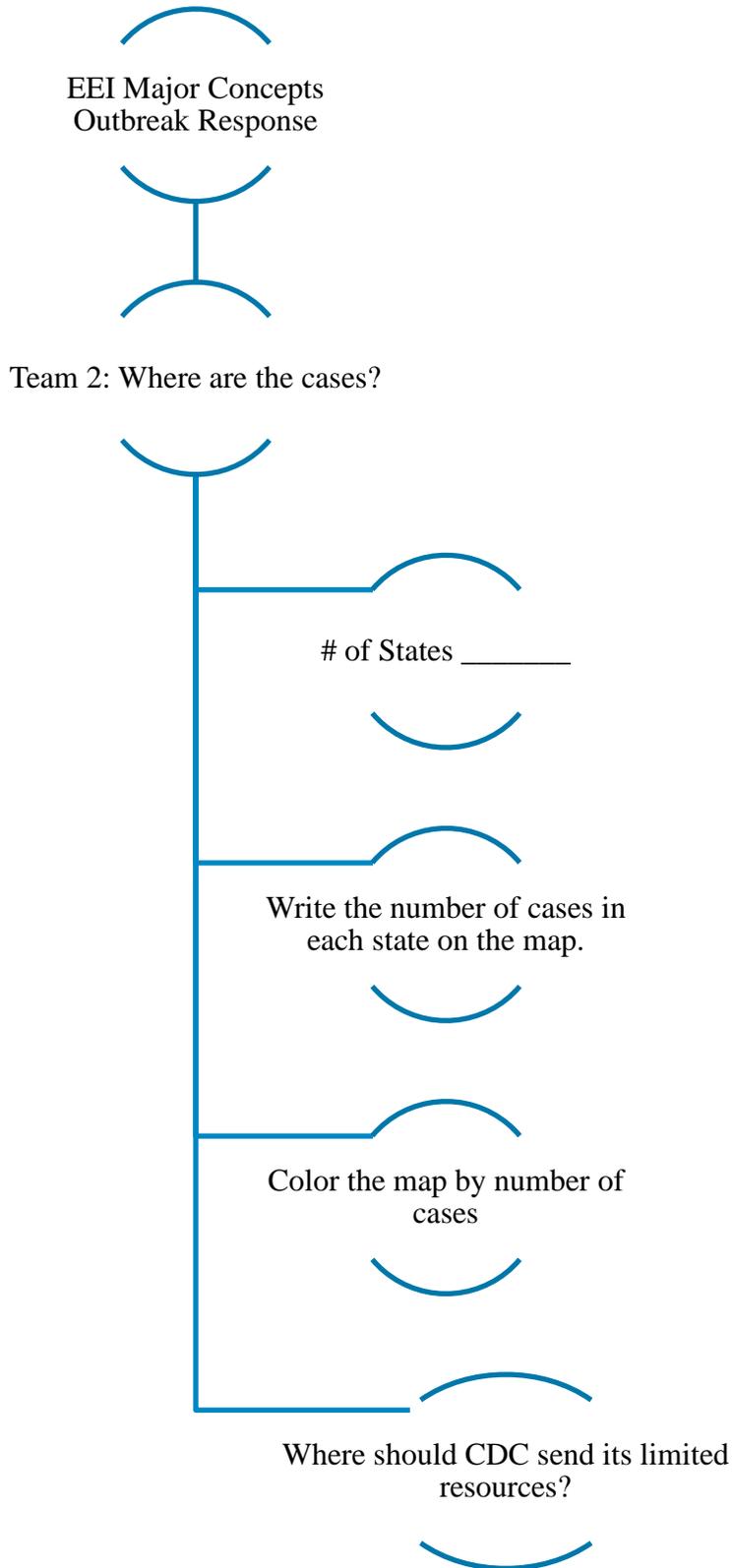
Team 1

Directions: Complete the flowchart by using the information provided in the scenario and the CDC website at <http://www.cdc.gov/hai/outbreaks/meningitis> if needed.



Team 2

Directions: Complete the flowchart by using the information provided in the scenario and the CDC website at <http://www.cdc.gov/hai/outbreaks/meningitis> if needed.



United States of America

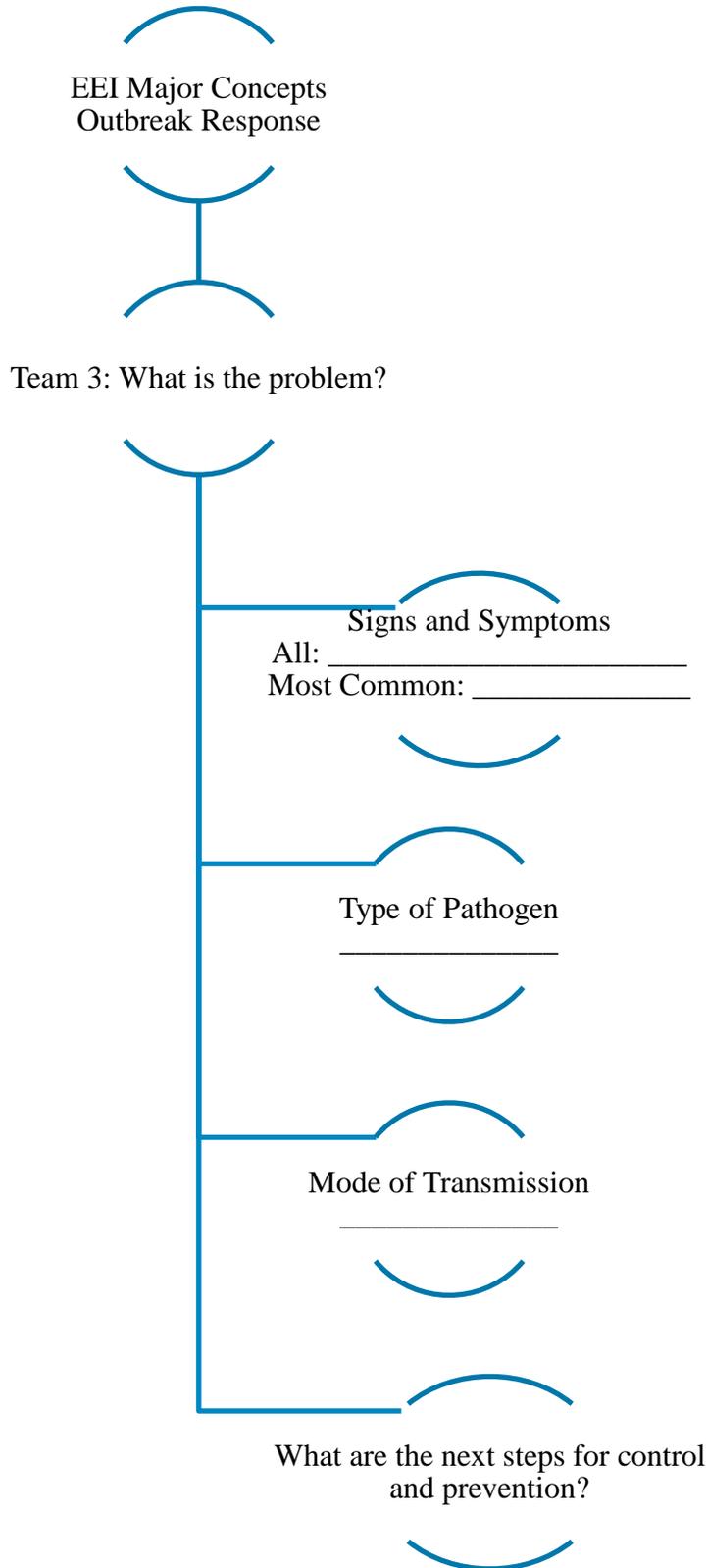


Key

Color	Cases
	1-11 Cases
	12-40 Cases
	41+ Cases

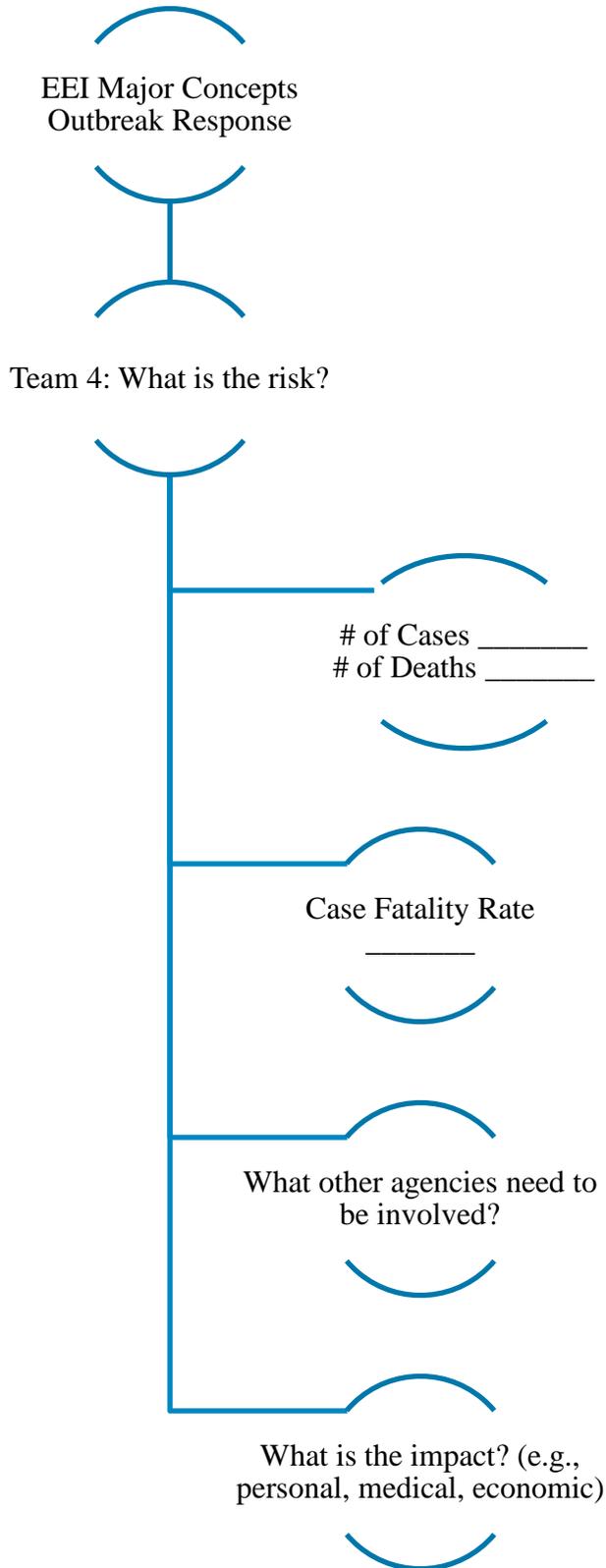
Team 3

Directions: Complete the flowchart by using the information provided in the scenario and the CDC website at <http://www.cdc.gov/hai/outbreaks/meningitis> if needed.



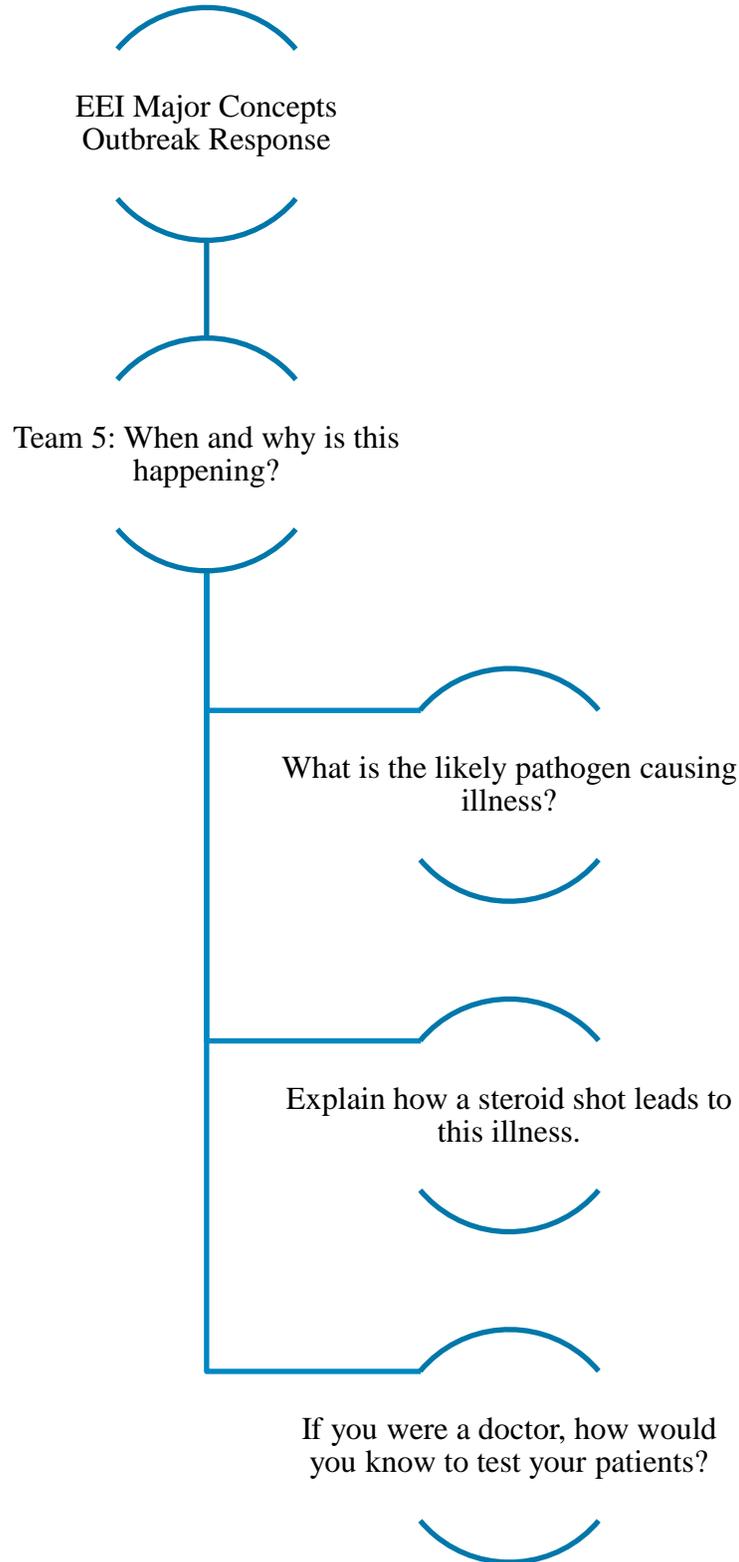
Team 4

Directions: Complete the flowchart by using the information provided in the scenario and the CDC website at <http://www.cdc.gov/hai/outbreaks/meningitis> if needed.



Team 5

Directions: Complete the flowchart by using the information provided in the scenario and the CDC website at <http://www.cdc.gov/hai/outbreaks/meningitis> if needed.



Part D: Putting it all together

Directions: With your group, create a complete flowchart of all of the information gathered. Use this information to complete the sections on case definition, critical thinking, and methods assessment.

Case Definition**Critical Thinking**

13 of 70 cases were confirmed to have growth of the fungus. Is this enough to initiate an emergency response? Why?

Method Assessment

Part E: Communicating information to the public

Directions: You have learned about the role of epidemiologists and how they look at a possible outbreak. Another role is to communicate information to the public, healthcare professionals, federal agencies, and anyone else who might need to be informed about an outbreak. Your job is to create a communication tool that covers the following criteria for the outbreak you have been studying.

Your communication tool will include

- Clinical information (i.e., signs, symptoms, risk factors)
- Suggested actions for those who might have been exposed
- CDC recommendations to the public to prevent future outbreaks

Some ideas for a communication tool include, infographics, a 45 second public service announcement (PSA), a pamphlet, a poster, or any other approved idea. Use the rubric as a guide to design your communication tool.

Rubric

Category	4	3	2	1	0
Knowledge Content	Includes all communication tool components	Includes 2 communication tool components	Includes 1 communication tool component	Little attempt to use any components	Not completed
Presentation of communication tool	Excellent use of graphics and effects to enhance the presentation	Good use of graphics and effects to enhance the presentation	Adequate use of graphics and effects to enhance the presentation	Makes use of graphics and effects to enhance the presentation	Not completed
Mechanics	No misspellings or grammatical errors	1-2 spelling mistakes or mechanical errors	3-4 spelling mistakes or mechanical errors	5+ spelling mistakes or mechanical errors	Not completed
Appropriateness	The medium is ideal for target audience	The medium is adequate for target audience	The medium is inadequate for target audience	The medium is not appropriate for target audience	Not completed

Worksheet 1B

What's in the Syringe? Guide

Name: _____

Date: _____

Directions: Use this page to help you complete the activity and find definitions for key terms.

Scenario: Help! Is it Safe for Me to Have Steroid Injections?

Tom, a high school senior, is the star basketball player and has suffered a knee injury. The doctor has suggested a steroid injection to decrease swelling on his knee. Tom's parents recently heard about contaminated steroid injections on the news. CDC had just released its findings about a multistate outbreak of fungal meningitis among patients who received contaminated steroid injections from the New England Compounding Center. Tom's parents are concerned about him receiving a steroid injection. They prefer to find an alternative method for treatment. Tom is frustrated. He has not heard about the contaminated steroid injections and wants to get back to playing basketball. Tom decides to call his cousin who is a CDC epidemiologist to learn more about the outbreak.

You are Tom's cousin and decide to use the Essential Elements of Information (EEI) to organize the details of the fungal meningitis investigation for Tom. EEI is situational information about people, systems, and services that is critical for an effective outbreak response. EEI flowcharts are completed as epidemiologists answer who, what, when, where, and why questions of an outbreak, and ultimately help the response team design a case definition and control the outbreak.

Task

Your task is to help Tom show his parents that it will be safe to have a steroid injection.

Part A: Key Terms (Homework)

Directions: Use the CDC website to define each key term.

Case Definition⁸

Answer: a set of uniformly applied criteria for determining whether a person should be identified as having a particular disease, injury, or other health condition. In epidemiology, particularly for an outbreak investigation, a case definition specifies clinical criteria and details of time, place, and person.

Epidemiologist

Answer: A person who studies and analyzes the patterns, causes, and effects of health and disease conditions in defined populations as well as the application of that study to control health problems.

Meningitis⁹

Answer: Meningitis is swelling of the protective membranes, or meninges, covering the brain and spinal cord. The swelling is usually caused by an infection with a bacteria or virus, but meningitis can also be caused by a fungus. Meningitis caused by a fungus is called fungal meningitis. The severity of illness and the treatment for meningitis differ depending on the cause, so knowing the specific cause of meningitis is important.

Fungal Meningitis

Answer: Fungal meningitis occurs when the protective membranes covering the brain and spinal cord are infected with a fungus. Fungal meningitis is rare and usually caused by the spread of a fungus through blood to the spinal cord.

Outbreak³

Answer: the occurrence of more cases of disease, injury, or other health condition than expected in a given area or among a specific group of persons during a specific period. Usually, the cases are presumed to have a common cause or to be related to one another in some way.

Risk Communication Specialist

Answer: A risk communicator provides information to help people make the best possible decisions for their health and well-being. This must be done in rapid timeframes and without knowing everything about the crisis.

Steroid Injection

Answer: Steroids (short for corticosteroids) are man-made drugs that closely resemble cortisol, a hormone that your body produces naturally. Steroids are injected into one or two local areas of inflammation allowing doctors to deliver a high dose of medication directly to the problem area.

⁸ Principles of Epidemiology, 3rd Edition: <http://www.cdc.gov/OPHSS/CSELS/DSEPD/SS1978/Glossary.html#C>

⁹ Definition: <http://www.cdc.gov/hai/outbreaks/patients/index.html>

Part B: Outbreak Information

Directions: Review the outbreak information provided. Use this information to complete Part C.

Fungal Meningitis Outbreak – Key Information

In September 2012, the Centers for Disease Control and Prevention (CDC), in collaboration with state and local health departments and the Food and Drug Administration (FDA), began investigating a multistate outbreak of fungal meningitis and other infections among patients who received contaminated preservative-free methylprednisolone acetate (MPA) steroid injections from the New England Compounding Center in Framingham, Massachusetts. Active case-finding efforts and extensive investigation into medications and medication lot numbers received by patients were used to evaluate the source of infection.

Fungal meningitis is not spread from person to person. Fungal meningitis can develop after a fungus spreads through the bloodstream from somewhere else in the body to the brain or spinal cord or from an infection next to the brain or spinal cord.

Signs and symptoms of fungal meningitis include fever, headache, stiff neck, nausea and vomiting, photophobia, and altered mental status.

If meningitis is suspected, samples of blood or cerebrospinal fluid (fluid surrounding the spinal cord) are collected and sent to a laboratory for testing. Knowing the specific cause of meningitis is important because the severity of illness and the treatment depend on the cause. To confirm fungal meningitis, specific lab tests can be performed, depending on the type of fungus suspected.¹⁰ The predominant fungus identified in patients is *Exserohilum rostratum*.¹¹ See table 3.



Figure 3: This photomicrograph reveals some of the morphology of the fungal organism, *Exserohilum rostratum*. CDC PHIL ID#15143

¹⁰ More information on fungal meningitis can be found at: <http://www.cdc.gov/meningitis/fungal.html>.

¹¹ More information on this outbreak can be found at: <http://www.cdc.gov/hai/outbreaks/meningitis.html>.

Table 1: Characteristics of patients (N = 70) with fungal infections following epidural steroid injection of methylprednisolone acetate from New England Compounding Center — United States, 2012.¹²

Characteristic	Number	(%)
Median age (yrs) (range)	68 (Range: 23-91)	
Sex		
Male	22	31
Female	48	69
Signs and Symptoms		
Headache	57	81
Fever	24	34
Nausea	21	30
Photophobia	7	10
Gait disturbance	3	4
Falls	8	11
Stroke	12	17
Fungus Identified		
Exserohilum species	13	9
Aspergillus species	1	1

Table 2: Cases and deaths with fungal infections linked to steroid injections – meningitis only cases.¹³

State	Meningitis Only	Deaths
TOTAL	234	64
Florida (FL)	22	7
Georgia (GA)	1	0
Idaho (ID)	1	0
Illinois (IL)	2	0
Indiana (IN)	30	11
Maryland (MD)	23	3
Michigan (MI)	23	19
Minnesota (MN)	10	1
North Carolina (NC)	1	1
New Hampshire (NH)	9	0
New Jersey (NJ)	30	0
New York (NY)	0	0
Ohio (OH)	12	1
Pennsylvania (PA)	1	0
Rhode Island (RI)	1	0
South Carolina (SC)	2	0
Tennessee (TN)	22	16
Texas (TX)	2	0
Virginia (VA)	42	5
West Virginia (WV)	0	0

¹²This table was derived from: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6141a4.htm>.

¹³ The complete data table is available at: <http://www.cdc.gov/hai/outbreaks/meningitis-map-large.html>

Table 3: CDC laboratory-confirmed organisms from recalled New England Compounding Center lots of preservative-free methylprednisolone acetate (MPA) lots recalled on September 26, 2012.¹⁴

MPA Lot #	Beyond Use	Fungi Isolated	Description
06292012@26	12/26/2012	<i>Exserohilum rostratum</i>	Known to cause human disease
08102012@51	2/6/2013	<i>Exserohilum rostratum</i>	Known to cause human disease
08102012@51	2/6/2013	<i>Cladosporium cladosporioides</i>	Does not grow at human body temperature
06292012@26	12/26/2012	<i>Rhodotorula laryngis</i>	Does not grow at human body temperature Not known to cause human disease
08102012@51	2/6/2013	<i>Rhodotorula laryngis</i>	Does not grow at human body temperature Not known to cause human disease
08102012@51	2/6/2013	<i>Rhizopus stolonifer</i>	Does not grow at human body temperature. Not known to cause human disease

Fungal Meningitis Outbreak – FDA News Release

FDA reports conditions observed at New England Compounding Center facility – Oct. 26, 2012

Today, the U.S. Food and Drug Administration released a copy of the FDA Form 483 issued to the New England Compounding Center (NECC). The FDA observed and has since confirmed contaminated products and listed a number of observations regarding conditions in the clean room at NECC’s Framingham, Mass. facility.

The investigators also observed problems with NECC’s ability to maintain its clean room, which is the enclosed space that is designed and maintained to have a controlled environment with low levels of airborne particles and surface contamination. Production of sterile drug products in a properly functioning and maintained clean room reduces the risk of the introduction of microbial contamination into the drug during processing, including filling into its final container.

The FDA issues a 483 at the end of an inspection when the investigators believe that they observed conditions or practices that, in their judgment, may indicate violations of the Federal Food, Drug, and Cosmetic Act, or related regulations. The 483 does not constitute a final FDA determination that any observation listed on the 483 is a violation of the Federal Food, Drug, and Cosmetic Act or any related regulations.

The FDA considers the 483 along with an Establishment Inspection Report (EIR), prepared by FDA investigators, and any other relevant information, including any responses received by the company. The agency then considers whether further action, if any, is appropriate. The inspection report for NECC has not been completed and is not being shared at this time.

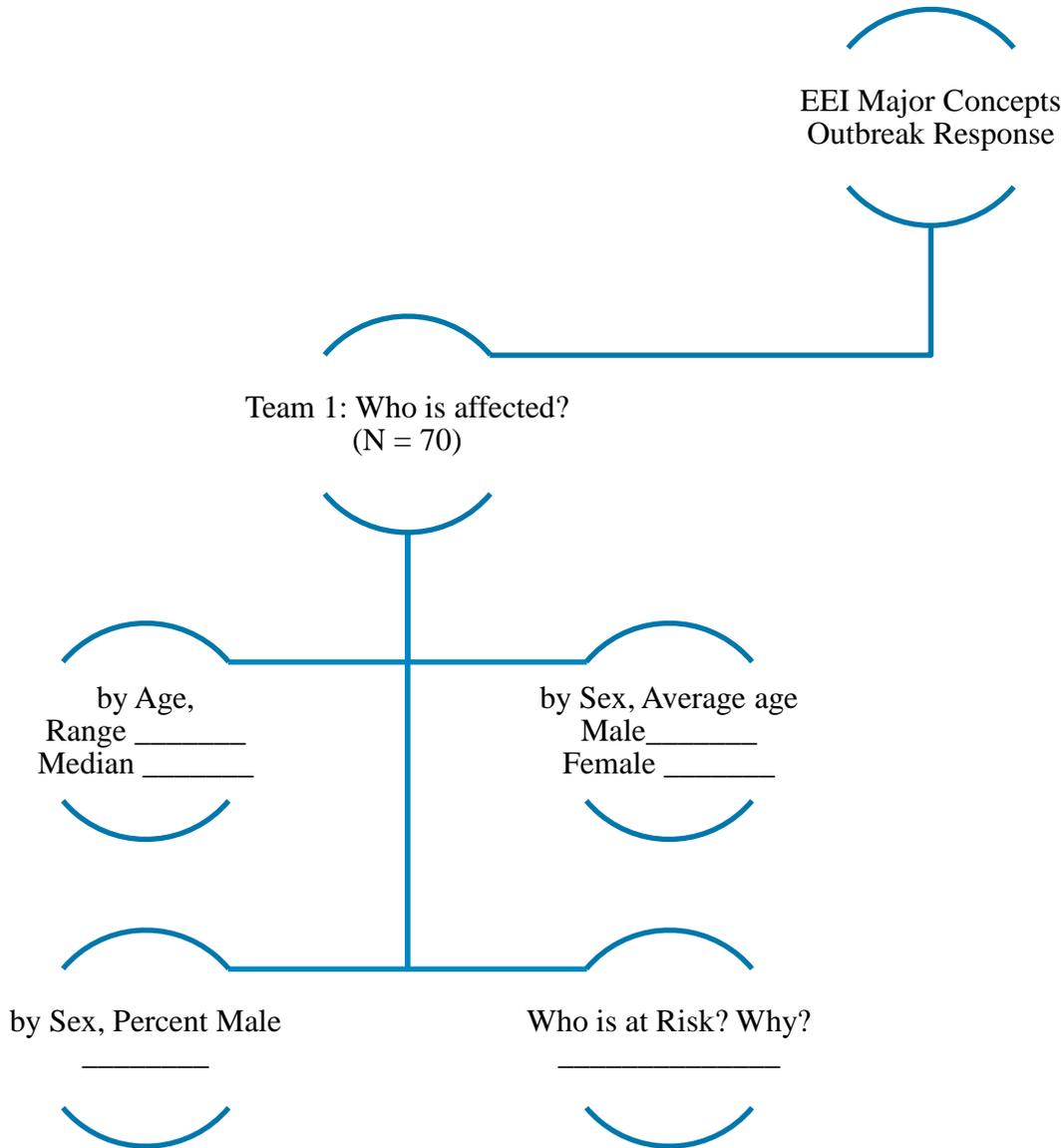
The FDA continues to work closely with the U.S. Centers for Disease Control and Prevention and state partners, including the Massachusetts Board of Registration in Pharmacy, to investigate the outbreak of fungal meningitis among patients who received NECC’s compounded preservative-free methylprednisolone acetate (80mg/ml), an injectable steroid.

¹⁴ This data is available at: <http://www.cdc.gov/hai/outbreaks/laboratory/index.html>.

Part C: Essential Elements of Information flowcharts

Team 1

Directions: Complete the flowchart by using the information provided in the scenario and the CDC website at <http://www.cdc.gov/hai/outbreaks/meningitis> if needed.



Team 1: Who is affected? (N = 70) Answer Key

Directions: Complete the flowchart by using the information provided in the scenario and the CDC website at <http://www.cdc.gov/hai/outbreaks/meningitis> if needed.

- by Age,
 - Range **Answer: 23-91**
 - Median **Answer: 68**

- by Sex, Average Age
 - Male **Answer: 22**
 - Female **Answer: 48**

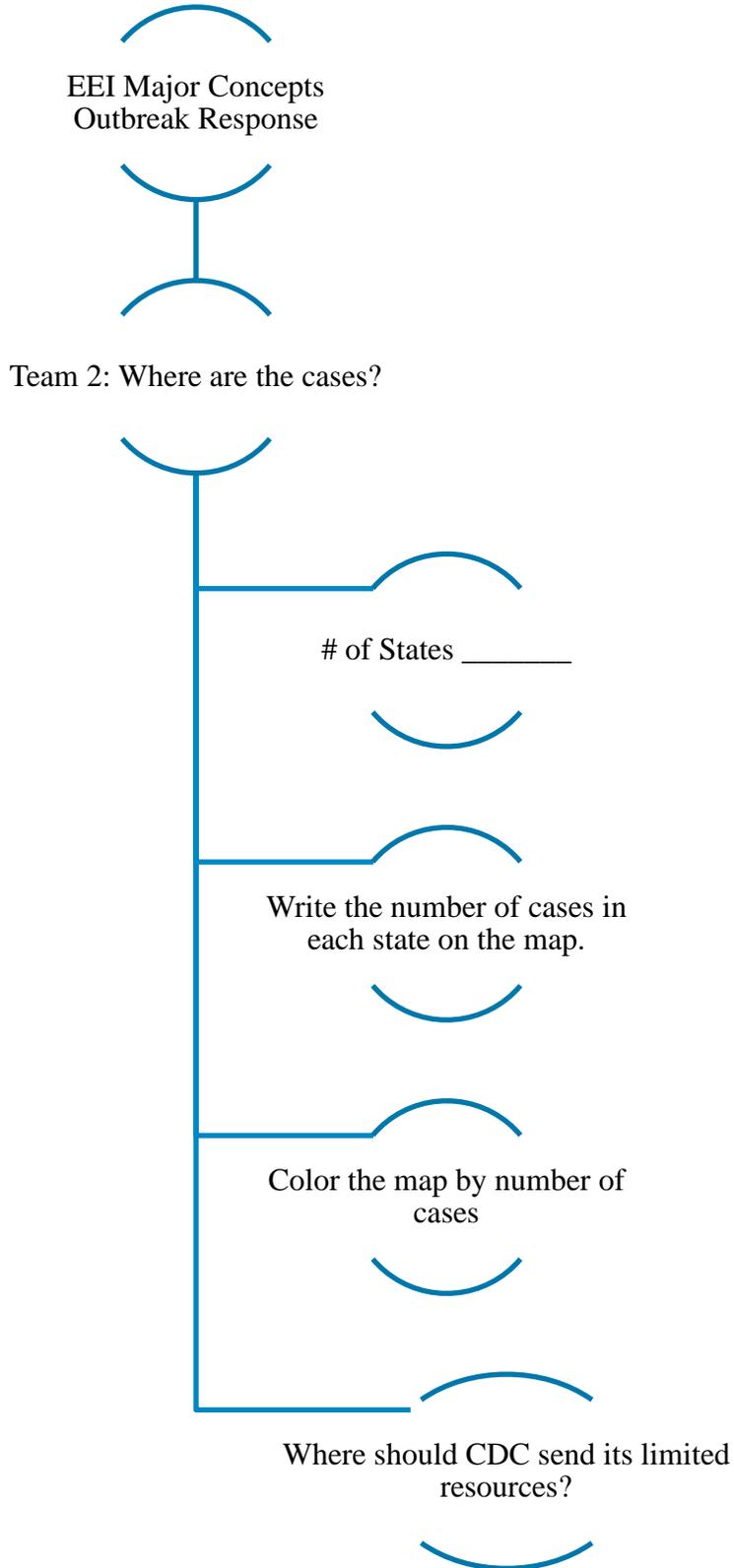
- by Sex, Percentage Male
 - Male **Answer: 69%**

- Who is at Risk? Why?

Answer: Answers will vary. Based on the information above, older male populations appear to be more vulnerable. This might be because of weakened immune responses or increased use of steroids. Female cases are older than male cases. This might be because males are more likely to receive steroid injections for sports-related injuries earlier in life and females are more likely to receive steroid injections for injuries later in life.

Team 2

Directions: Complete the flowchart by using the information provided in the scenario and the CDC website at <http://www.cdc.gov/hai/outbreaks/meningitis> if needed.



United States of America



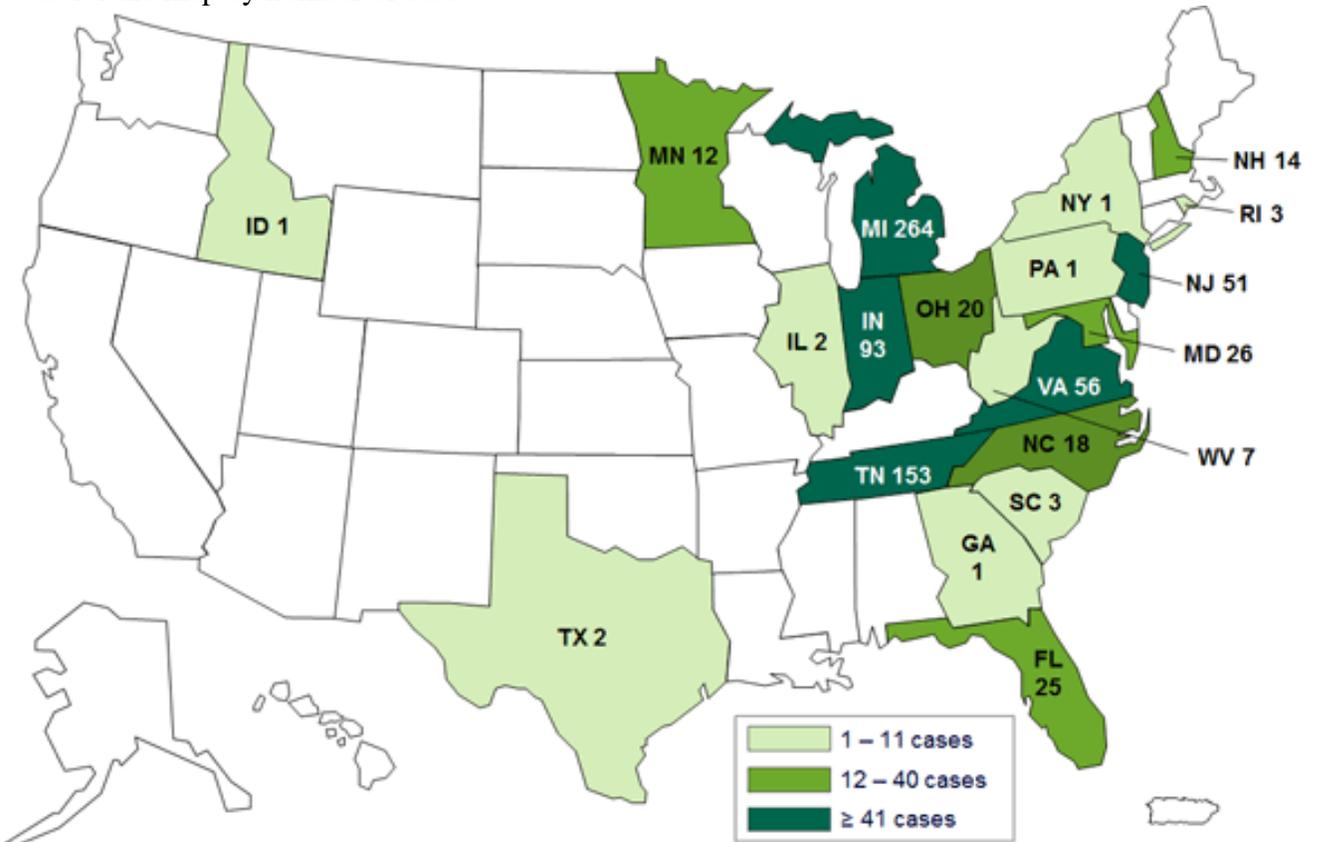
Key

Color	Cases
	1-11 Cases
	12-40 Cases
	41+ Cases

Team 2: Where are the cases? Answer Key

Directions: Complete the map by using the information provided in the scenario and the CDC website at <http://www.cdc.gov/hai/outbreaks/meningitis> if needed.

- Write the number of cases in each state.
- Color the map by number of cases

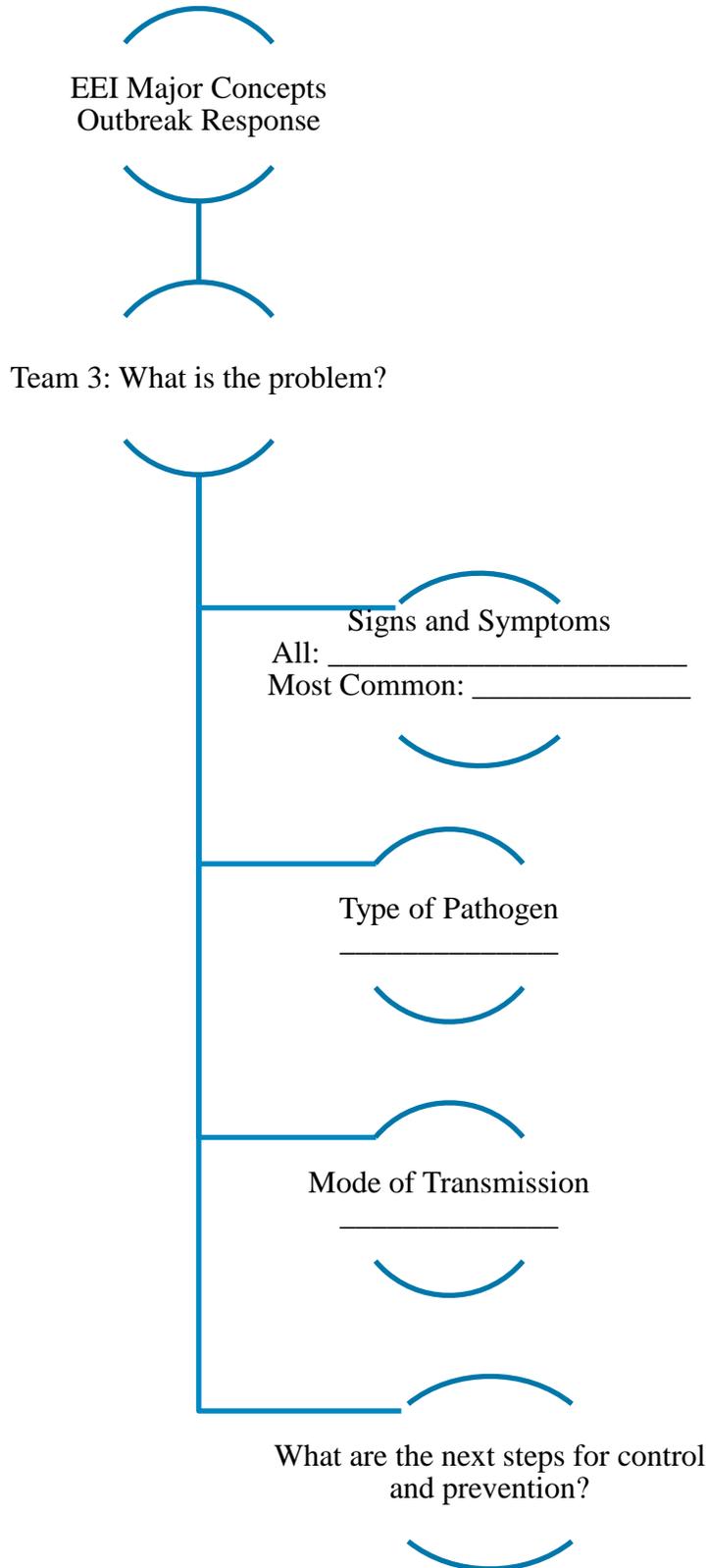


Based on the map, where might CDC send its limited resources?

Answer: High numbers of cases (41+) occurred in Michigan, Indiana, New Jersey, Virginia, and Tennessee. Depending on the resources available by the local and state public health departments, resources would likely be sent to these states. Other states with limited resources might also receive aid.

Team 3

Directions: Complete the flowchart by using the information provided in the scenario and the CDC website at <http://www.cdc.gov/hai/outbreaks/meningitis> if needed.

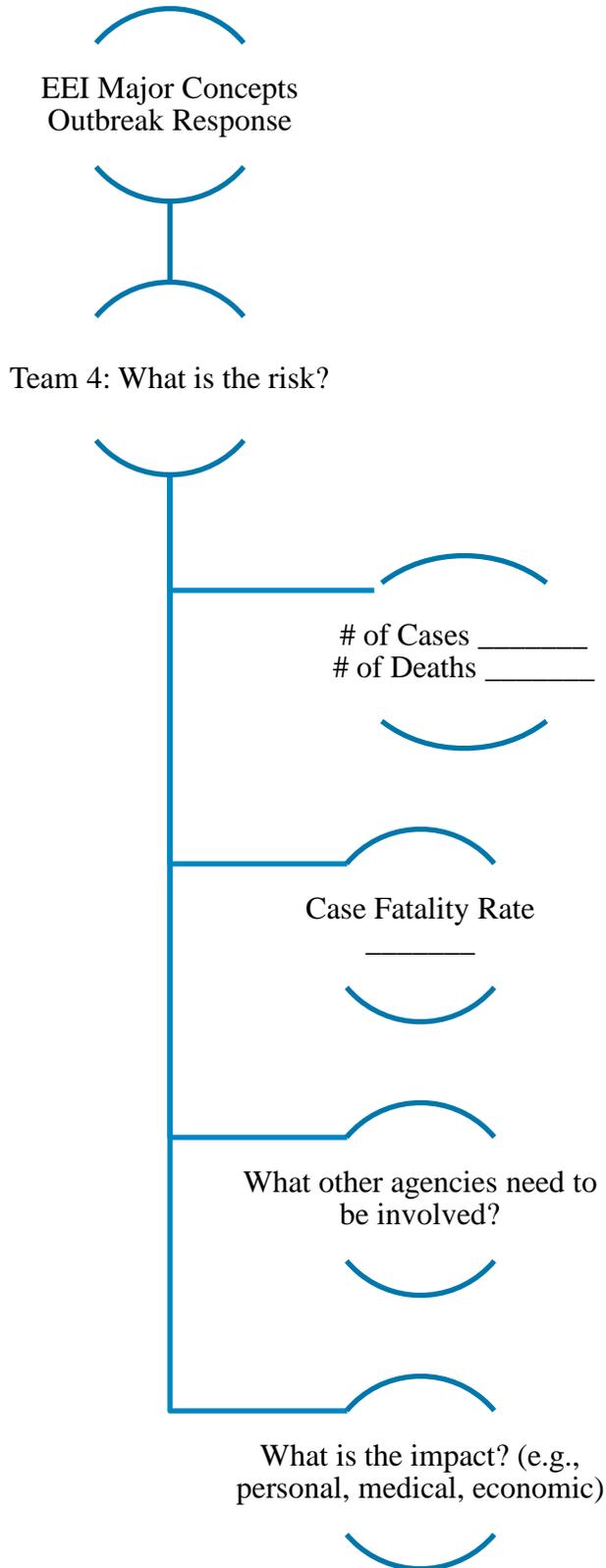


Team 3: What is the problem? Answer Key

- Signs and Symptoms
 - All
Answer: Signs and symptoms of fungal meningitis include headache (81%), fever (34%), nausea (30%), photophobia (10%), gait disturbance (4%), falls (11%), and stroke (17%).
 - Most Common
Answer: Signs and symptoms of fungal meningitis include headache (81%).
- Type of Pathogen
Answer: Fungus.
- Mode of Transmission
Answer: Steroid injection (vehicle transmission). Fungal meningitis develops after the fungus is injected and spreads through the bloodstream to the brain or spinal cord or from an infection next to the brain or spinal cord. Note: The mechanism in which the fungus spreads through the bloodstream to the brain or spinal cord is somewhat unknown. It is likely that there is a mix of local infection in the injected area (e.g., joint, epidural space) and bloodstream spread, if there was an infection documented at a distal site.
- What are the next steps for control and prevention?
Answer: Treat cases: Fungal meningitis is treated with long courses of high dose antifungal medications, usually given through an IV in the hospital. The length of treatment depends on how strong the immune system is and the type of fungus that caused the infection. For people with weak immune systems, like those with AIDS, diabetes, or cancer, treatment is often longer. Identify and destroy contaminated steroid vials.

Team 4

Directions: Complete the flowchart by using the information provided in the scenario and the CDC website at <http://www.cdc.gov/hai/outbreaks/meningitis> if needed.

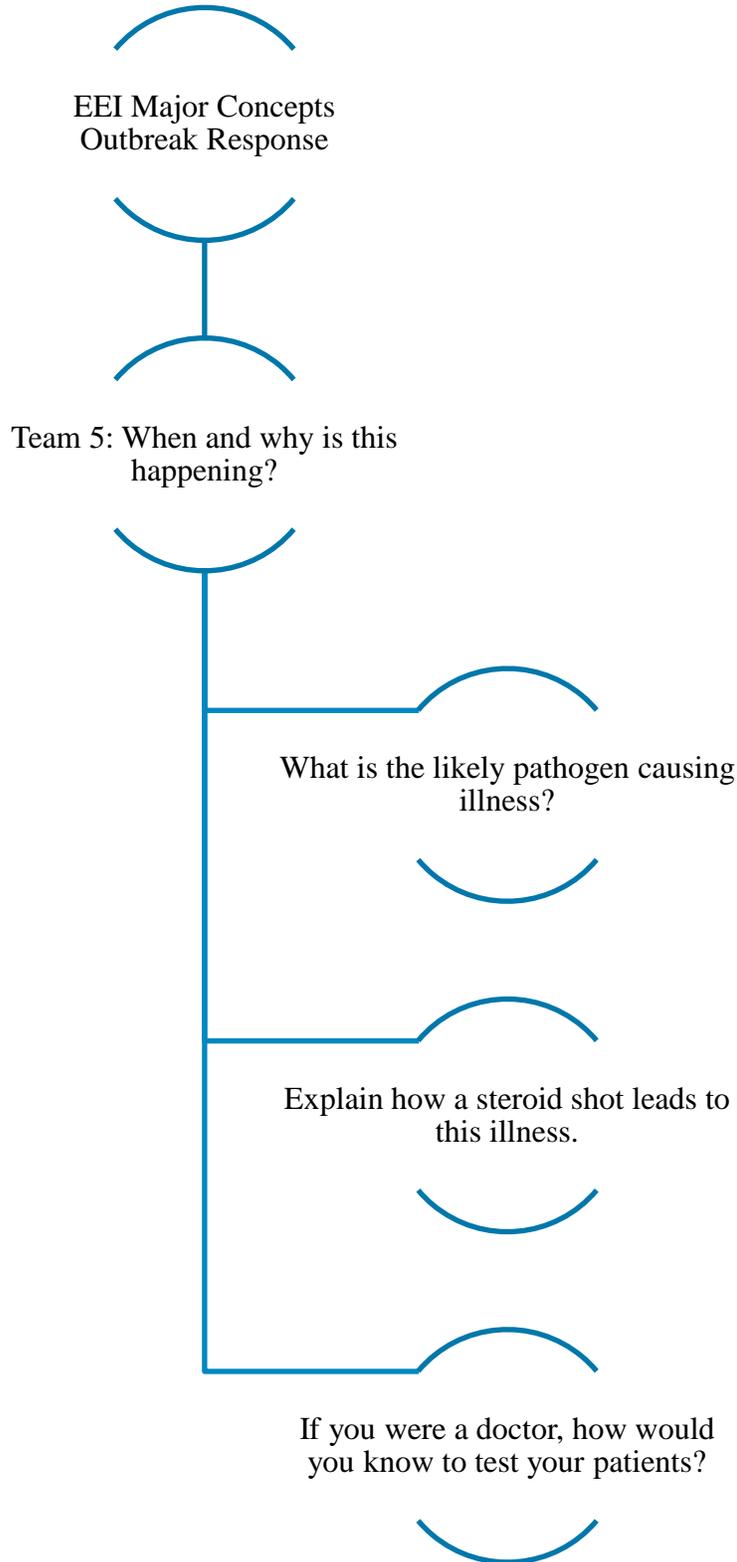


Team 4: What is the risk? Answer Key

- # of Confirmed Cases
Answer: 234
- # of Deaths
Answer: 64
- What other agencies need to be involved?
Answer: FDA, state and local health departments, laboratories, hospitals
- What is the impact:
Answer: Personal impact might include death, loss of wages, hospitalization costs, and long term health complications. Economic impacts might include cost of the investigation and recall, research, regulation/policy changes. Medical impact could include increased need for medical treatment and services and patient concern about future use of steroids. It could also lead to the need for additional training in laboratory storage and injection techniques.

Team 5

Directions: Complete the flowchart by using the information provided in the scenario and the CDC website at <http://www.cdc.gov/hai/outbreaks/meningitis> if needed.

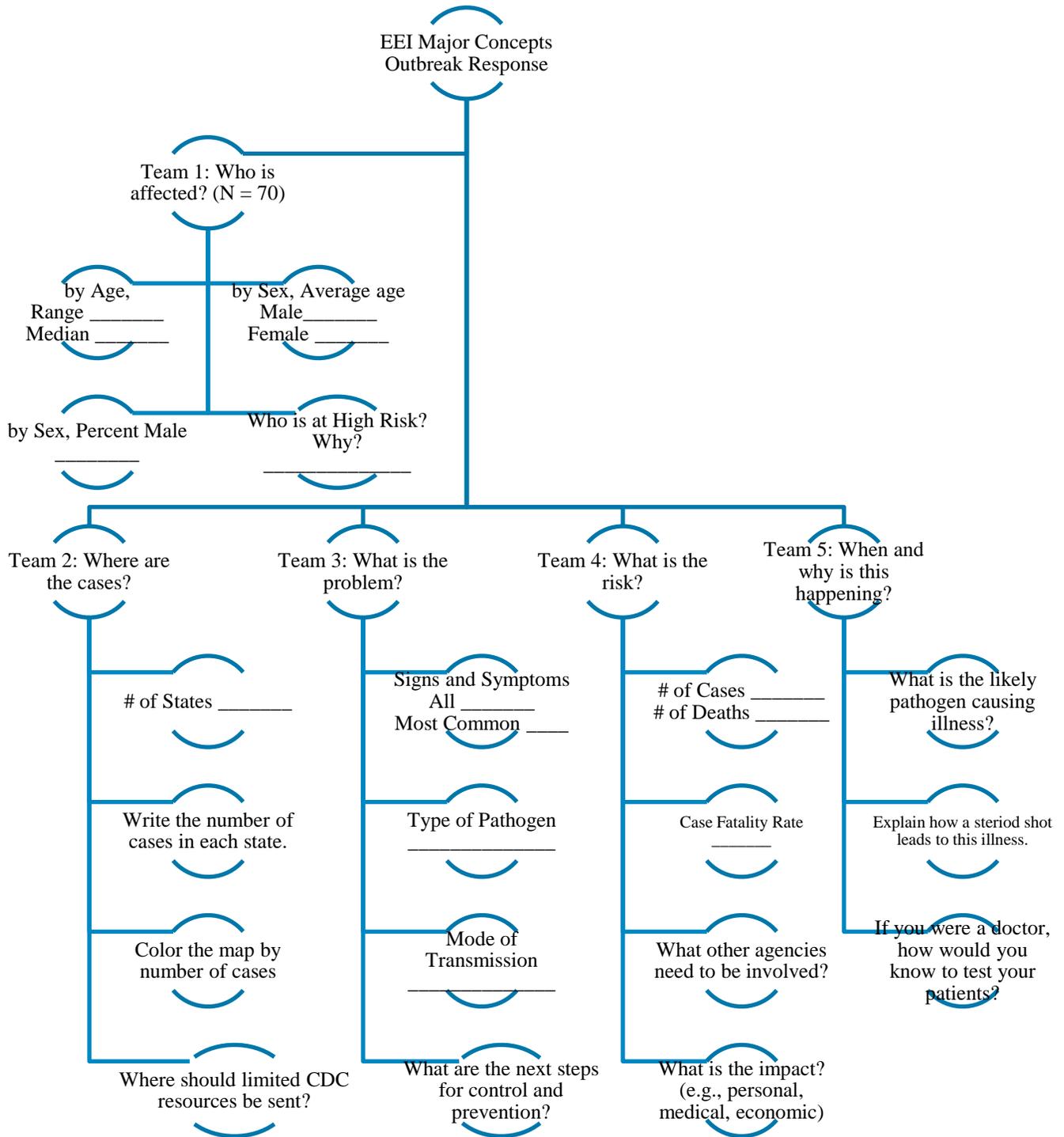


Team 5: When and why is this happening? Answer Key

- What is the likely pathogen causing illness?
Answer: The fungus causing fungal meningitis in this outbreak is likely *Exserohilum rostratum* since it was predominantly in most cases.
- Explain how a steroid shot leads to this illness.
Answer: Vials of a steroid that were infected with the fungus were injected. The fungus spreads through the bloodstream to the brain or spinal cord. The infection causes meningitis, or inflammation (swelling) of the protective membranes covering the brain and spinal cord known as the meninges.
- If you were a doctor, how would you know to test your patients?
Answer: If patients have received a steroid injection from the infected vials and showed symptoms. In this outbreak, asymptomatic people who were exposed were contacted to ensure they were clear on the symptoms to look for and what to do if they had symptoms. There was also outreach to physicians to education them on treatment.

Part D: Putting it all together

Directions: With your group, create a complete flowchart of all of the information gathered. Use this information to complete the sections on case definition, critical thinking, and methods assessment.



Case Definition

Answer: A person who received a preservative-free methylprednisolone acetate (MPA) injection, with preservative-free MPA that definitely, or likely, came from one of the following three lots produced by the New England Compounding Center (NECC) [05212012@68, 06292012@26, 08102012@51], and subsequently developed signs and symptoms of meningitis, including headache, fever, nausea, photophobia, gait disturbance, falls, and stroke following epidural or paraspinal injection after May 21, 2012.

Note: You may choose to have students break up the case definition by its components: person, place, time, and clinical features.

Note: The actual case definition for this outbreak is provided below and can be found at: <http://www.cdc.gov/hai/outbreaks/clinicians/index.html>. For simplicity of this exercise, students should focus on fungal meningitis and developing the above case definition.

Actual Case Definition: A person who received a preservative-free methylprednisolone acetate (MPA) injection, with preservative-free MPA that definitely, or likely, came from one of the following three lots produced by the New England Compounding Center (NECC) [05212012@68, 06292012@26, 08102012@51], and subsequently developed any of the following:

- Meningitis of unknown etiology following epidural or paraspinal injection after May 21, 2012;
- Posterior circulation stroke without a cardioembolic source and without documentation of a normal cerebrospinal fluid (CSF) profile, following epidural or paraspinal injection after May 21, 2012;
- Osteomyelitis, abscess or other infection (e.g., soft tissue infection) of unknown etiology, in the spinal or paraspinal structures at or near the site of injection following epidural or paraspinal injection after May 21, 2012; or
- Osteomyelitis or worsening inflammatory arthritis of a peripheral joint (e.g., knee, shoulder, or ankle) of unknown etiology diagnosed following joint injection after May 21, 2012.

If the case was not evidenced by culture, histopathology, or molecular assay of a fungal pathogen associated with the clinical syndrome, it was considered a probable case. If it was evidenced, it was considered a confirmed case.

Critical Thinking

13 of 70 cases were confirmed to have growth of the fungus. Is this enough to initiate an emergency response? Why?

Answer: Although 13 cases appears to be a small number of cases, fungal meningitis is rare. The cases were also distributed across several states and regions. Because of the rarity and wide-spread distribution, CDC was asked to support the multistate outbreak investigation.

Method Assessment

Answer: During an outbreak, EEI helps focus epidemiologic questions that can be time sensitive so that investigators are not overwhelmed with data that are not pertinent or data that could cause a delay in pinpointing the case definition and source of the outbreak. EEI also helps keep all team members focused on gathering the necessary information.

Part E: Communicating information to the public

Directions: You have learned about the role of epidemiologists and how they look at a possible outbreak. Another role is to communicate information to the public, healthcare professionals, federal agencies, and anyone else who might need to be informed about an outbreak. Your job is to create a communication tool that covers the following criteria for the outbreak you have been studying.

Your communication tool will include

- Clinical information (i.e., signs, symptoms, risk factors)
- Suggested actions for those who might have been exposed
- CDC recommendations to the public to prevent future outbreaks

Some ideas for a communication tool include, infographics, a 45 second public service announcement (PSA), a pamphlet, a poster, or any other approved idea. Use the rubric as a guide to design your communication tool.

Rubric

Category	4	3	2	1	0
Knowledge Content	Includes all communication tool components	Includes 2 communication tool components	Includes 1 communication tool component	Little attempt to use any components	Not completed
Presentation of communication tool	Excellent use of graphics and effects to enhance the presentation	Good use of graphics and effects to enhance the presentation	Adequate use of graphics and effects to enhance the presentation	Makes use of graphics and effects to enhance the presentation	Not completed
Mechanics	No misspellings or grammatical errors	1-2 spelling mistakes or mechanical errors	3-4 spelling mistakes or mechanical errors	5+ spelling mistakes or mechanical errors	Not completed
Appropriateness	The medium is ideal for target audience	The medium is adequate for target audience	The medium is inadequate for target audience	The medium is not appropriate for target audience	Not completed